REMARKS

Claims 10-16, 24 and 25-27 are pending. Claims 10, 11 and 13 have been amended. Claims 26 and 27 have been added. Support for amended claims 10 and 11 can be found in the specification at page 10, line 27 to page 11, line 4. Claim 13 has been amended to correct a duplication of the term "amphetamine." Support for new claim 26 can be found in the specification at page 10, line 27 to page 11, line 4 and page 11, lines 5-23. Support for new claim 27 can be found in the specification at page 10, line 27 to page 11, line 4 and page 17, lines 21-28.

Reconsideration of this application is respectfully requested.

Rejection of claims 10-16 and 24-25 under 35 U.S.C. § 103(a)

The rejection of claims 10-16, 24 and 25 as obvious over WO 01/26623 ("Horrobin") is respectfully traversed. Horrobin discloses the use of a selective norepinephrine reuptake inhibitor together with phenylalanine or tyrosine for the treatment of chronic fatigue syndrome ("CFS"), fibromyalgia syndrome ("FMS") and symptoms associated therewith, including pain. Horrobin is primarily directed to compounds that inhibit the reuptake of norepinephrine alone, but also discloses dual norepinephrine/serotonin reuptake inhibitors such as milnacipran. The Examiner contends that it would have been obvious to use milnacipran to treat pain because Horrobin discloses the use of milnacipran to treat symptoms, which include pain. Further, the Examiner contends that dependent claims to adjunctive treatment with additional compounds, specific dosages, and dosage formulations were matters of routine optimization known to one of ordinary skill in the art. Claims 24 and 25, directed to kits, were obvious, according to the Examiner, because inclusion of a package insert is mandated by 21 CFR §201.57 and unit dose packaging is routine in the pharmaceutical art.

As amended, claims 10-16, 24 and 25 would not have been obvious to one of ordinary skill in the art because Horrobin teaches away from the use of milnacipran without co-administration of phenylalanine or tyrosine. Horrobin discloses the case history of a patient with CFS, FMS and irritable bowel syndrome ("IBS") who was not effectively treated with various drugs including "serotonin reuptake inhibiting and noradrenaline reuptake inhibiting antidepressants" (Horrobin, page 8). The patient only improved following administration of lofepramine, a selective

noradrenaline reuptake inhibitor, in combination with L-phenylalanine. *Id.* Horrobin does not disclose or suggest that milnacipran administration, without co-administration of a neurotransmitter precursor such as phenylalanine or tyrosine, would be effective. In fact, Horrobin suggests that any treatment other than a noradrenaline reuptake inhibitor in combination with a neurotransmitter precursor such as phenylalanine, tyrosine or tryptophan would fail. Horrobin discloses at page 8, lines 16 to 19 that the patient with FMS, CFS and IBS "was given almost all conceivable treatments over the years, including many types of non-steroidal anti-inflammatory drugs, both tricyclic and serotonin reuptake inhibiting and noradrenaline reuptake inhibiting antidepressants, and even steroids. Some of these treatments produced transient effects but these never lasted." Thus, there was no reasonable expectation of success for the treatment of pain with milnacipran, without co-administration of a neurotransmitter precursor such as phenylalanine, tyrosine or tryptophan, in combination with any other compound, at any dosage or in any dosage formulation. Further, claims 24 and 25 would not have been obvious because there would have been no motivation to include a package insert teaching a method for treatment that had no reasonable expectation of success.

Accordingly, this rejection should be withdrawn.

The rejection of claims 10-16 under 35 U.S.C. § 103(a)

Claims 10-16 stand rejected under 35 U.S.C. 103(a) as obvious over teachings of Moreau et al. (DRUGU AN 1992-39596) ("Moreau") in view of Woerz zum Thema (DRUGU AN 1983-01770) ("Woerz"). According to the Examiner, Moreau discloses the use of antidepressants to treat pain and Woerz discloses that milnacipran is an antidepressant agent. Thus, the Examiner contends, it would have been obvious to use milnacipran to treat pain and yield the instant method. According to the Examiner, the dependent claims, which recite dosage regimens and dosages, are obvious because these were matters of routine optimization. Dependent claims to milnacipran administered adjunctively with another active agent are obvious according to the Examiner because Woerz discloses that neuroleptics and opiates are used to treat pain.

This rejection is respectfully traversed. Moreau does not suggest the use of antidepressants to treat pain nor does Moreau suggest that milnacipran is an antidepressant agent. Moreau discloses the electrophysiological effects and clinical tolerance of intravenous milnacipran compared to imipramine-like antidepressant agents. Woerz does not suggest or motivate one of

ordinary skill in the art to modify what is taught in Moreau to arrive at the claimed use of milnacipran for the treatment of pain by teaching the use of drugs, including "antidepressants, e.g. doxepine, amitryptyline, imipramine and clomipramine" for the treatment of cancer pain. All of the exemplified antidepressants in Woerz are tricyclic antidepressants. Milnacipran is not a tricyclic antidepressant. Thus, Moreau and Woerz do not disclose or suggest the use of milnacipran (which is not a tricyclic antidepressant) for the treatment of pain. Withdrawal of the obviousness rejection of claims 10-16 is believed to be in order.

The rejection of claims 24-25 under 35 U.S.C. § 103(a)

Claims 24 and 25 stand rejected under 35 U.S.C. 103(a) as obvious over EMBASE AN 1998129084 ("'084") or EMBASE AN 90228858 ("'858"). According to the Examiner, '084 discloses the use of milnacipran in ambulatory and hospital settings, and '858 discloses the use of milnacipran in hospitalized patients. The Examiner contends that claim 24 would have been obvious in light of these references because a package insert teaching a method of use is mandated by 21 CFR §201.57. Dependent claim 25 recites unit dose packaging. Such packaging is routine in the pharmaceutical art, according to the Examiner, and therefore would be obvious, especially in an institutionalized setting such as disclosed in '084 and '858.

It would not have been obvious to assemble a kit including milnacipran with instructions for treating pain because, in accordance with the arguments above, methods for treating pain with milnacipran are nonobvious. Withdrawal of the rejection of claims 24 and 25 under 35 U.S.C. §103(a) is requested.

The provisional rejection of claims 26-55 for double-patenting

Applicant acknowledges that claims 10-16 have been provisionally rejected for obviousness-type double-patenting over claims 1-7 of U.S. Patent No. 6,602,911; claims 10-16 have been provisionally rejected for obviousness-type double-patenting over claims 1-5 of U.S. Patent No. 6,635,675; and claims 10-16 and 24-25 have been provisionally rejected for obviousness-type double-patenting over claims 26-55 of co-pending Application No. 10/623,431. Since this is a provisional rejection, Applicants defer addressing the rejection until allowable subject matter has

been identified in this application. If this rejection remains at that time, Applicants will address the rejection.

The Information Disclosure Statement

According to the Examiner, several references, which were included in an Information Disclosure Statement were not considered because copies were not present in the file of the parent application. A Supplemental Information Disclosure Statement, form PTO/SB/08 and copies of references EP 0759299, FR 2752732, WO 97/35584, WO 99/59593, WO 00/32178, WO 02/053140, Dwight, Goodnick, Ninan, Nutt & Johnson, and Rao are enclosed. Applicant respectfully requests that the references be considered and made of record in this application. We have not identified a reference corresponding to MEDLINE, et al., "Treatment of chronic fatigue syndrome with sibutramine ..." PCT Int'l Appl. 14 (09/28/2000).

Conclusion

No new matter has been added by these amendments. In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

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By_____

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